PhD PROJECT SYNOPSIS
School of Life Sciences

Project title: Regulation of Extracellular Vesicles and microRNAs in Glioblastoma Multiforme – novel roles for Peptidylarginine Deiminases and Cannabidiol

Cross College/Department Project? YES

If YES, name of other College/Departments: Collaboration with Research Centre for Optimal Health and Cancer Research Group

Name of research group/centre: Tissue Architecture and Regeneration Research Group

Background to research and synopsis (200 words max)

Glioblastoma multiforme (GBM) is the most common and aggressive form of primary malignant brain tumour in adults, with poor prognosis. Extracellular vesicles (EVs) are key-mediators for cellular communication through transfer of proteins and genetic material. Cancers, such as GBM, use EV release for drug-efflux, pro-oncogenic signalling, invasion and immunosuppression; thus the modulation of EV release and changes in EV cargo, including microRNAs, are of considerable clinical relevance.

Our recent publications show that EV release in GBM and other cancers can be targeted via the Peptidylarginine-deiminase (PAD) mediated pathway and by Cannabidiol (CBD) and that these may work in synergy, albeit via different mechanisms. We have shown both changes in amounts of EVs released, as well as a shift of a pro-oncogenic to an anti-oncogenic microRNA signature in GBM in response to PAD-inhibitor and CBD treatment.

The proposed project will establish how EV subpopulations and key-microRNAs can be selectively modulated with single or combinatory EV-inhibitors, to increase GBM susceptibility to therapy. Furthermore, changes in selected mitochondrial, nuclear and invadopodia related proteins will be investigated.

This project will create a platform for enhanced treatment efficacy in GBM and may also be translatable to other types of cancer.

The student will learn a range of state-of the art skills relating to extracellular vesicle and microRNA analysis and take part in the University Graduate School and College Doctoral Research Development Programme.

Supervisory Team:

Supervisor Name	Role (DoS, 2nd/ 3rd Supervisor)	No. of successful PhD/ MPhil supervisions	Current number of students supervised in academic year 2019/20 (FTE)	Have you been a DoS for a UoW-funded Research Scholar in last 5 years? i.e. since academic year 2013/14?
Sigrun Lange	1st	2 PhD co-supervisions	1 MSc extended project	No
Pinar Usyal-Onganer	2nd	1 PhD co-supervison	2 MSc extended projects	No

		5 MRes supervisions		
Jimmy Bell	3rd	>20	2	No

Recent publications by supervisors that are relevant to the project:

Kosgodage, US, **Uysal-Onganer P**, MacLatchy A, Nicholas AP, Inal JM, **Lange S** (2019). Peptidylarginine Deiminases Post-translationally deiminate Prohibitin and modulate Extracellular Vesicle Release and microRNAs in Glioblastoma Multiforme. Int J Mol Sci 20(1):103.

Kosgodage US, **Uysal-Onganer P**, MacLatchy A, Mould R, Nunn AV, Guy GW, Kraev I, Chatterton NP, Thomas EL, Inal JM, **Bell JD, Lange S** (2019). Cannabidiol Affects Extracellular Vesicle Release, miR21 and miR126, and Reduces Prohibitin Protein in Glioblastoma Multiforme Cells. Transl Oncol. 12(3):513-522.

Kosgodage US, Mould R, Henley AB, Nunn AV, Guy GW, Thomas EL, Inal JM, **Bell JD, Lange S** (2018). Cannabidiol (CBD) Is a Novel Inhibitor for Exosome and Microvesicle (EMV) Release in Cancer. Front Pharmacol. 9:889.

Kosgodage US, Trindade RP, Thompson PT, Inal JM, **Lange S** (2017). Chloramidine/Bisindolylmaleimide-I-Mediated Inhibition of Exosome and Microvesicle Release and Enhanced Efficacy of Cancer Chemotherapy. Int J Mol Sci.18(5).

Lange S, Gallagher M, Kholia S, Kosgodage US, Hristova M, Hardy J, Inal JM (2017). Peptidylarginine Deiminases – Roles in Cancer and Neurodegeneration and Possible Avenues for Therapeutic Intervention via Modulation of Exosome and Microvesicle (EMV) Release? Int J Mol Sci. 18(6): 1196.

Kholia S, Jorfi S, Thompson PR, Causey CP, Nicholas AP, Inal J, **Lange S** (2015). A Novel Role for Peptidylarginine Deiminases (PADs) in Microvesicle Release: A Therapeutic Potential for PAD Inhibitors to Sensitize Prostate Cancer Cells to Chemotherapy. J Extracellular Vesicles; 4:26192.

Informal enquiries (email address of Director of Studies) and any web links that prospective applicants would be referred to:

Director of Studies: Dr Sigrun Lange, Senior Lecturer in Molecular Pathology, Lead of Tissue Architecture and Regeneration Research Group: S.Lange@westminster.ac.uk;

Information on the supervisory team:

https://www.westminster.ac.uk/about-us/our-people/directory/lange-sigrun

https://www.westminster.ac.uk/tissue-architecture-and-regeneration-research-group

https://www.westminster.ac.uk/about-us/our-people/directory/uysal-onganer-pinar

https://www.westminster.ac.uk/about-us/our-people/directory/bell-jimmy

To make your application:

https://digital.ucas.com/courses/details?coursePrimaryId=2d83fe4a-9366-6394-f3e8-71ebd586d6f0&courseOptionId